Coexistence of Optic Nerve Head Drusen and Combined Hamartoma of the Retina and Retinal Pigment Epithelium in a Taiwanese Male

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We report the case of a 38-year-old male patient with a 1-year history of progressively blurred vision in his left eye. He visited our clinic and underwent a series of ophthalmologic examinations including computed tomography, fluorescein angiography and optical coherence tomography. The final diagnosis was optic nerve head drusen and combined hamartoma of the retina and retinal pigment epithelium in his left eye.

Key Words: combined hamartoma, optic nerve head drusen, retinal pigment epithelium
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The term "combined hamartoma" was first used by Gass in 1973 [1]. It is a relatively uncommon lesion made up of variable amounts of retinal pigment epithelial, vascular, and glial components [1,2]. Affected individuals typically present with symptoms during early adulthood, characterized by unilateral painless loss of vision in the affected eye. Visual acuity (VA) loss may result from direct involvement of the optic nerve, the papillomacular bundle, or the fovea caused by the lesion. However, associated epiretinal membrane formation, or subretinal and intraretinal exudation from the vascular component of the lesion may also contribute to decreased VA [2].

Optic nerve head drusen (ONHD) is a condensation of hyaline-like material within the substance of the optic nerve head. The condition is bilateral in about 75% of cases, with a prevalence of 0.3–2% in the general population, and it is more common in Caucasians with fair complexions [3]. To our knowledge, the coexistence of ONHD and combined hamartoma of the retina and retinal pigment epithelium (CHR-RPE) is rare [2]. We describe a Taiwanese male with ONHD and CHR-RPE.

Case Presentation

A 38-year-old male patient was referred to our clinic in June 2004 following a painless decrease in vision in his left eye for at least 1 year. There was no contributory medical history in the patient or his family. His best-corrected VA was 20/20 in the right eye and 20/400 in the left eye. The refraction status was –0.5D in both eyes. Motility was within normal limits with no sign of strabismus or proptosis. There was a mild left relative afferent pupillary defect. Slit lamp examination of the anterior chamber and anterior vitreous was unremarkable in both eyes. Applanation tonometry demonstrated an intraocular pressure of 13 mmHg in the right eye and 15 mmHg in the left eye. A dilated fundus examination showed a normal right

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fundus. However, the left eye showed a pinkish-yellow elevation of the optic nerve head with a blurred disc margin and a slightly elevated grayish peripapillary lesion with some areas of pigmentation, which obscured the optic disc margins and extended to the papillomacular region. Peripapillary hard exudation and subretinal hemorrhage were detected inferior to the optic disc. The retinal vessels appeared to be stretched and tortuous with epiretinal glial tissue (Figure 1A). Red-free photography revealed autofluorescence from the optic nerve head without the administration of fluorescein (Figure 1B). Fluorescein angiography showed a partially blocked early choroidal fluorescence, retinal vascular tortuosity (Figure 1C), and a moderate late hyperfluorescence from leaking retinal capillaries in the region of the lesion (Figure 1D). B-scan ultrasonography displayed optic nerve head elevation at normal sensitivity, and the lesion remained sonoreflective, even after the other tissues had been removed from view by lowering the sensitivity. Computed tomography showed a discrete, rounded calcification in the left eye confined to the superficial layers of the optic disc (Figure 2A). Optical coherence tomography (OCT) of his left eye showed retinal folding, macular edema and disorganized retinal layers (Figure 2B).

Results of routine laboratory tests including blood cell counts, serum calcium, alkaline phosphatase, serum phosphate, parathyroid hormones, blood protein levels, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and autoimmune factors were all within normal limits. Based on the above findings, a diagnosis of ONHD and CHR-RPE was made. Management was conservative and the patient was observed monthly for follow-up care. During the following 2.5 years, the size of the tumor and the area of exudative retinal detachment seemed to increase and there was some epiretinal membrane formation surrounding the macular area (Figure 1E). Fluorescence angiography showed retinal vascular tortuosity and late hyperfluorescence of the lesion. However, no evident subretinal neovascularization was observed (Figure 1F).

Discussion

In this case, the diagnosis of CHR-RPE was based on the following findings.

- Ophthalmoscopic examination revealed an ill-defined, partly pigmented, gray-white peripapillary mass lesion with surrounding vascular tortuosity and overlying gliosis.
- Fluorescein angiography demonstrated early hypofluorescence corresponding to the pigmented area and late phase with leakage from the retinal vascular abnormalities and staining of the entire lesion.

The term hamartoma refers to the abnormal proliferation of a tissue or group of tissues normally present in a particular area. The first pathologic report of CHR-RPE was published in 1958 by Dr Georgiana Theobald and colleagues. On microscopic examination, the pigment epithelium was seen to proliferate into the retinal stroma and the lesion contained many fine capillaries and glial cells [4]. In the case of combined hamartomas, either melanocytic, vascular or glial tissues usually dominate the clinical picture. Therefore, some CHR-RPEs appear to contain prominent vascular elements which might account for the surrounding exudative retinal edema. Some, however, appear to contain predominantly glial elements which lead to vitreoretinal interface changes with the formation of epiretinal membrane [1,2]. In our case, the predominant elements were vascular and glial elements, because the major findings were retinal vascular tortuosity, exudation, hemorrhage and epiretinal membrane. The differential diagnosis of CHR-RPE includes choroidal melanoma, choroidal nevi, retinoblastoma, melanocytoma, capillary hemangioma and post-inflammatory conditions [2]. The diagnosis of CHR-RPE usually depends on a detailed fundus examination and fluorescein angiography. Recently, OCT has become the adjuvant diagnostic tool of choice and important features of CHR-RPE detected by OCT include a thickened retinal mass with hyperreflective surface, epiretinal membrane and disorganized retinal structure [5].

The diagnosis of ONHD is as follows.

- The optic nerve head becomes elevated with blurred margins, obscuring the physiologic cup.
- Red-free photography shows autofluorescence from the drusen.
- B-scan ultrasound reveals high echoic focus at the optic nerve head.
- Computed tomography shows intraorbital calcifications at the level of the optic nerve head.

ONHD consists of calcified material in the substance of the optic nerve head. The presence of drusen may

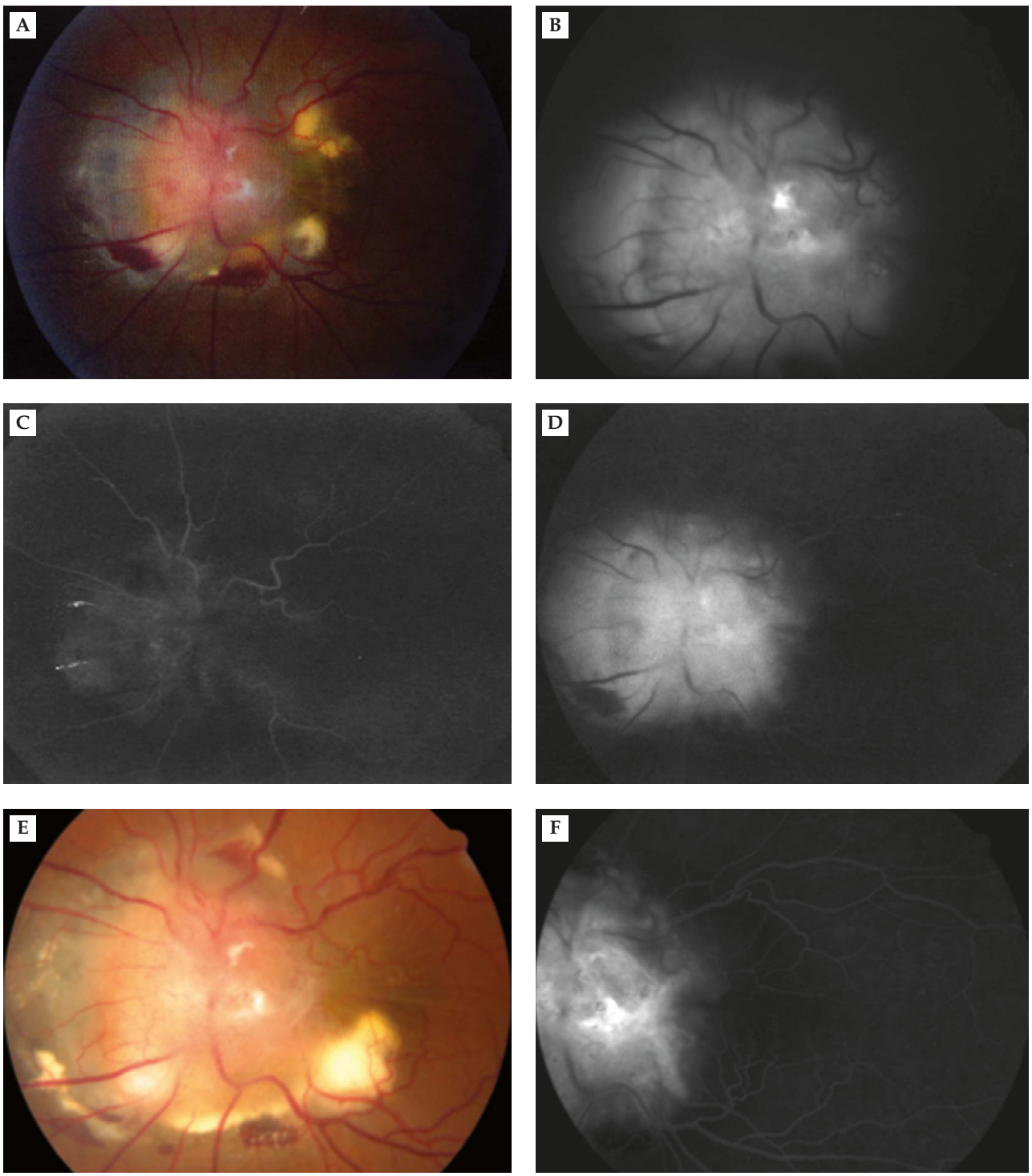

Figure 1. *(A) Color fundus photography of the left eye shows a slightly elevated optic nerve head with blurred and irregular disc margins. There is a grayish-pink mass involving the optic nerve head and macula. Prominent exudation, intraretinal hemorrhage and tortuosity of the retinal vessels are present. (B) Before administration of fluorescein, red-free photography shows autofluorescence from the drusen. (C) Early phase angiogram shows hypofluorescence corresponding to the pigmented area and tortuous retinal vessels. (D) In late phase, there is diffuse hyperfluorescence of the lesion secondary to leakage from the retinal vascular abnormalities. (E) Color fundus photography of the left eye taken 2 years later shows a slightly enlarged tumor and more prominent peripapillary exudation. There is epiretinal membrane contracture around the macular area. (F) Late phase angiogram reveals leakage over the area of the hamartoma. There is no evident subretinal neovascularization noted.*

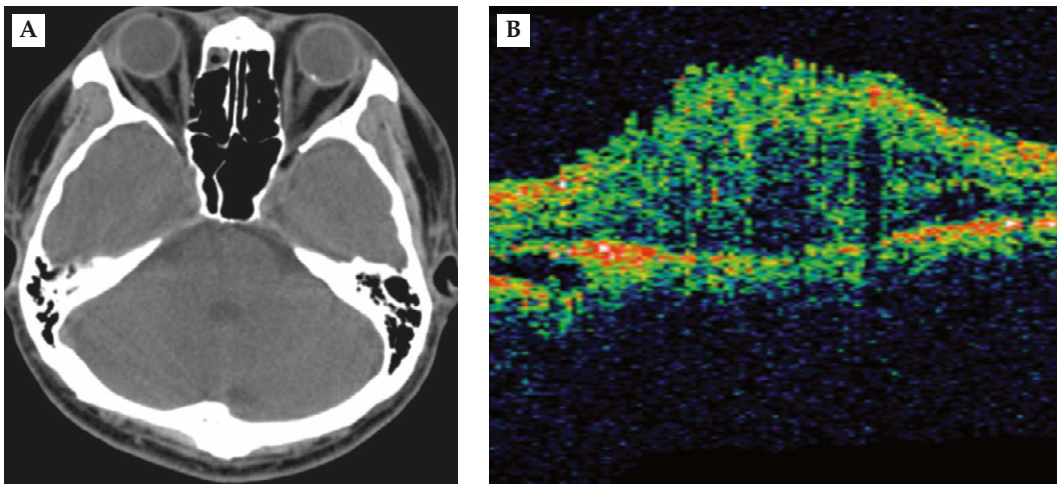

Figure 2. *(A) Computed tomography shows a calcifying mass in the left optic disc. (B) Vertical optical coherence tomography scan reveals elevated, hyperreflective lesion with underlying hyporeflective shadowing. The retinal thickness is 300 μm.*

cause blurring of the optic disc margins and may be mistaken for papilledema. Autofluorescence confirms this surface drusen in over 96% of cases [6]. The etiology is unknown, but ultrastructurally drusen appears to be a result of degenerative axonal products. It has been suggested that small scleral foramina impede normal axoplasmic flow, leading to stasis. Abnormal axonal metabolism then leads to deposition of calcium crystals in the extracellular space. Continuous calcifications of these microbodies coalesce to form drusen [7].

The coexistence of ONHD and CHR-RPE in this case was a rare finding. There were only two patients with associated ONHD in Schachat et al's study of 60 cases of CHR-RPE [2]. The correlation between these two tumors was not clear, because both tumors were believed to be congenital in nature. Some studies have shown an association between ONHD and other ocular conditions such as anterior ischemic optic neuropathy, retinal hemorrhage, retinitis pigmentosa, or angioid streaks. At present, there is no specific treatment for CHR-RPE or ONHD, only for the complications resulting from them. For example, laser photocoagulation or photodynamic therapy can be considered for subretinal neovascularization, and membrane peeling for the formation of epiretinal membrane [2,8,9].

In conclusion, we report an uncommon case of unilateral coexistence of ONHD and CHR-RPE. Further research is needed to develop effective treatments for these conditions.

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單側視神經盤疣合併視網膜色素層缺陷瘤 — 病例報告

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我們提出一個病例報告關於一位 38 歲的台灣男性發覺左眼視力減退達 1 年之久。這位病人接受一系列的檢查包括了眼部電腦斷層攝影，底螢光攝影以及視網膜光學同調斷層掃描之後發現是一個視神經盤疣合併視網膜色素層缺陷瘤。我們針對此一罕見疾病做一文獻回顧及探討。

關鍵詞：缺陷瘤，視神經盤疣，視網膜色素層

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